Journal of the American College of Cardiology
Vol. 60, No. 18, 2012

Published by Elsevier Inc.
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2012.07.034

EDITORIAL COMMENT

Left Bundle Branch Block After Transcatheter Aortic Valve Implantation

Inconsequential or a Clinically Important Endpoint?*

Antonio Colombo, MD, Azeem Latib, MD
Milan, Italy

The close proximity of the aortic valve complex to the His bundle makes the intraventricular conduction tissue susceptible to damage during transcatheter aortic valve implantation (TAVI) (1,2). New-onset left bundle branch block (LBBB) is the most frequently observed conduction abnormality, which is explained by the very superficial location of the left bundle branch in the uppermost part of the leftward ventricular septum. The left bundle branch may be easily traumatized by manipulation of catheters or stiff wires, balloon valvuloplasty, valve implantation, or post-dilatation, and more than one-half of the conduction abnormalities during TAVI have been reported to occur prior to valve implantation (3).

See page 1743

The pathology of these conduction disturbances may be transient inflammation, edema, ischemia, or mechanical stress, which may explain why many recover. There are limited data on the clinical consequences of new-onset LBBB after TAVI. Indeed, clinical dilemmas often faced by physicians managing patients post-TAVI are whether the new-onset LBBB could progress to complete heart block (CHB) and whether LBBB negatively affects left ventricular (LV) function and prognosis. With regard to the latter, LBBB has been identified as a predictor of poorer clinical outcomes, both in the surgical literature (after surgical aortic valve replacement) (4) and in the general cardiology literature (5), which begs the question as to whether we have underestimated the prognostic significance of new-onset LBBB after TAVI.

In this issue of the *Journal,* Urena et al. (6) report the "true" incidence, predictors, and clinical consequences of persistent LBBB after the implantation of the balloon-expandable valve (Sapien and Sapien XT, Edwards Lifesciences LLC, Irvine, California) in 202 consecutive patients. In interpreting their results, particularly in the context of other published literature, it is important to note that the investigators studied a "clean" population and excluded patients with baseline ventricular conduction disturbances or a history of permanent pacemaker implantation (PPI). The main findings were:

- New-onset LBBB occurred in 30.2% of patients immediately after Edwards implantation and had resolved in 37.7% at discharge and 57.3% at 1-year follow-up.
- Longer baseline QRS duration and a more ventricular positioning of the prosthesis predicted persistent LBBB.
- LBBB at discharge was associated with higher risks for syncope, CHB, and PPI (20% vs. 0.7%) but not sudden death or mortality, at 1-year follow-up.
- Persistent LBBB was associated with a decrease of $4.75 \pm 8.02\%$ in LV ejection fraction (LVEF) and a poorer New York Heart Association functional class at 1-year follow-up.

This represents one of the largest published studies to specifically evaluate the incidence, progression, predictors, and clinical significance of new-onset LBBB after TAVI. As demonstrated in Table 1, the incidence of new-onset LBBB (if calculated in a similar way by excluding patients with pre-existing LBBB, right branch bundle block, and PPI) varies considerably, from 25% to 85% (mean: 60.4% [95% confidence interval (CI): 56.9% to 63.9%] in 738 patients from 11 studies) (1–3,7–14) after implantation of the self-expandable CoreValve (Medtronic Inc, Minneapolis, Minnesota) and from 8% to 30% (mean: 21.9% [95% CI: 18.3% to 26.0%] in 438 patients from 5 studies) (6,14–17) after the implantation of a balloon-expandable valve. With regard to the time course of LBBB, this conduction disturbance usually occurs during TAVI but can occur afterwards in 2% to 8% (18, 19). It is reversible by discharge in up to one-half of patients treated with a self-expandable valve and in about one-third of patients treated with a balloon-expandable valve. These findings suggest that the injury to the left bundle branch sometimes may be transient. The fact that the incidence of LBBB is greater following implantation of the self-expandable valve may be a consequence of the fact that this valve type tends to land deep in the LV outflow tract more frequently compared to the balloon-expandable valve. Considering the close anatomic relationship between the annulus and left bundle branch, it is not

*Editorials published in the *Journal of the American College of Cardiology* reflect the views of the authors and do not necessarily represent the views of *JACC* or the American College of Cardiology.

From San Raffaele Scientific Institute and EMO-GVM Centro Cuore Columbus, Milan, Italy. Dr. Colombo has reported that he has no relationships relevant to the contents of this paper to disclose. Dr. Latib is on the advisory board of Medtronic.

Table 1 Summarizing Incidence Rates,* Time Course, and Requirements for Permanent Pacing in Patients With New-Onset LBBB After TAVI

Valve Type/Study First Author (Ref. #)	N	Excluded	New-Onset LBBB Immediately After TAVI	New-Onset LBBB In-Hospital	Resolved at Discharge	Persistent LBBB at Discharge	Persistent LBBB at 1 Yr	PPI After New-Onset LBBB
Self-expandable valve†								
Khawaja (1)	243	58	—	56.8 (105/185)	N/A	N/A	N/A	32.4 (34/105)
Piazza (2)	39	9	—	53.3 (16/30)	56.3 (9/16)	23.3 (7/30)‡	N/A	N/A
Nuis (3)	65	12	67.9 (36/53)	75.5 (40/53)	30 (12/40)	49.1 (26/53)	N/A	5 (2/40)
Jilaihawi (7)	30	8	—	50 (11/22)	N/A	N/A	N/A	0
Fraccaro (8)	64	17	—	59.6 (28/47)	10.7 (3/28)	53.2 (25/47)	N/A	N/A
Guetta (9)	70	28	—	78.6 (33/42)	27.3 (9/33)‡	38.1 (16/42)	N/A	24.2 (8/33)
Tzikas (10)	27	1	—	53.8 (14/26)	N/A	53.8 (14/26)	N/A	N/A
Chorianopulos (11)	130	27	77.7 (80/103)	84.5 (87/103)	6.3 (5)	79.6 (82/103)	N/A	13.8 (12/87)
Calvi (12)	162	23	54.7 (76/139)	56.8 (79/139)	6.6 (5)	46 (64/139)	N/A	12.7 (10/79); 6.3 (4/64); 17.7 (14/79)§
Munoz-Garcia (13)	61	37	—	25 (6/24)	0	25 (6/24)	N/A	
Balloon-expandable valve‖			—					
Urena (6)	202	0	28.2 (57/202)	30.2 (61/202)	37.7 (23/61)	12.4 (25/202)	36 (9/25)	13.1 (8/61); 20 (5/25); 21.3 (13/61)§
Gutiérrez (15)	33	5	—	21.4 (6/28)	33.3 (2/6)	13.3 (4/30)	3.3 (1/30)‡	0
Godin (16)	69	17	—	17.3 (9/52)	66.7 (6/9)‡	5.8 (3/52)‡	N/A	11.1 (1/9)
Sinhal (17)	106	22	—	8.3 (7/84)	42.9 (3/7)	4.8 (4/84)	N/A	0
Both types included								
Aktug (14)							N/A	17.5 (7/40)
Self-expandable	72	5	—	40.3 (27/67)	55.6 (15/27)	17.9 (12/67)	—	—
Balloon-expandable	82	10	—	18.1 (13/72)	46.2 (6/13)	9.7 (7/72)‡	—	—
Roten (18)	41/26¶	14/10¶	34.9 (15/43)	41.9 (18/43)‡	11.1 (2/18)‡	23.3 (10/43)‡	N/A	33.3 (6/18)
Erkapic (19)	36/14¶	12	—	52.6 (20/38)	N/A	N/A	N/A	N/A

Values are % (n/N). *Incidence rates may differ from those in the original articles, as they were calculated with the exclusion of patients with pre-existing LBBB, right branch bundle block, or PPI implantation (if not already excluded by the investigators), when these data were reported. †Trademark: CoreValve (Medtronic Inc, Minneapolis, Minnesota). ‡Only 1-month data available. §Values for in-hospital, follow-up, and overall. ‖Trademark: Sapien (Edwards Lifesciences LLC, Irvine, California). ¶For self-expandable and balloon-expandable valves, respectively.

LBBB = left bundle branch block; N/A = not available; PPI = permanent pacemaker implantation; TAVI = transcatheter aortic valve implantation.

surprising that the depth of valve implantation has been the most frequently identified predictor of LBBB in patients with either of the 2 prostheses (2,6,12,14). Although speculative, high valve implantation may reduce the risk for LBBB. It would be interesting to study whether implantation in a high position is associated with a low occurrence of LBBB even with the self-expandable valve. The other predictor identified in this study, longer baseline QRS, was probably a marker of underlying degenerative conduction system disease in this elderly population.

The present study provides us with important data to respond to 2 clinically important questions.

First, could new-onset LBBB progress to CHB? Based on the present study, new-onset LBBB was the only factor associated with PPI following TAVI (21.3% of patients overall). A clinically relevant but unappreciated finding was that 1 in 5 patients discharged with LBBB required PPI during follow-up. Similarly, 20.3% (95% CI: 16.4% to 24.9%) of patients with new-onset LBBB after the implantation of a self-expandable valve may require PPI. This information is original because "new-onset LBBB" has not been previously identified as a predictor for CHB or PPI in other studies, probably because these studies included only baseline and procedural variables in the predictive multivariate models.

Second, can and how does new-onset LBBB affect long-term outcomes? Urena et al. (6) reported that new-onset LBBB worsens LVEF and functional status, which may seem provocative at first glance. However, LBBB has been shown to be associated with deterioration of LV systolic and diastolic function, worsening heart failure and has been identified as a predictor of increased mortality in patients with isolated LBBB as well as those with structural heart disease. Indeed, the sicker the patient, the greater the impact of this conduction disturbance on adverse outcomes (5,20). Zannad et al. (5) eloquently summarized the pathophysiologic mechanisms as: LBBB, intraventricular asynchrony, reduced pump function, neurohormonal activation, asymmetric hypertrophy, and dilatation, followed by deteriorating LV function and emerging heart failure. Another factor that provides further evidence of the negative effects of LBBB and that is of particular importance to TAVI patients is the impact of right ventricular (RV) pacing, which shares common features with the depolarization and mechanical activity observed in LBBB. The MOST (Mode Selection Trial) (21) and the DAVID (Dual Chamber and

VVI Implantable Defibrillator) trials (22) showed that there was a significant association between RV pacing and the risk for hospitalization for heart failure in patients with normal and depressed LVEF, respectively. Thus, it is not surprising that LBBB may be deleterious in patients with TAVI who, by definition, have structural heart disease. Finally, it should be remembered that restoration of the ventricular activation sequence by cardiac resynchronization therapy opposes the various mechanisms that lead to ventricular dilation and ventricular remodeling.

The main limitation of the current study was the sample size and that it did not provide information on predicting which patients with new-onset LBBB will develop CHB or have worsening LV function and benefit from preventative therapy. If these findings are confirmed in larger series, the practical message is clear: Irrespective of the device implanted, we should avoid positioning the aortic prosthesis too ventricularly. Patients with new-onset LBBB post-TAVI should be kept on continuous electrocardiographic monitoring while in-hospital, and those discharged with persistent LBBB should have regular Holter monitoring. In these editors' opinion, there are certain subgroups of patients with persistent LBBB or RV pacing post-TAVI who should be closely monitored and even considered for cardiac resynchronization therapy if other causes, such as prosthesis malfunction, paravalvular leak, or coronary ischemia, have been excluded. These patients include those with pre-TAVI LV dysfunction without improvement in LVEF post-TAVI, those who continue to have symptomatic heart failure post-TAVI, and those with worsening LVEF on serial echocardiography.

Reprint requests and correspondence: Dr. Antonio Colombo, EMO-GVM Centro Cuore Columbus, Via Buonarroti 48, 20145 Milan, Italy. E-mail: info@emocolumbus.it.

REFERENCES

1. Khawaja MZ, Rajani R, Cook A, et al. Permanent pacemaker insertion after CoreValve transcatheter aortic valve implantation: incidence and contributing factors (the UK CoreValve Collaborative). Circulation 2011;123:951–60.
2. Piazza N, Onuma Y, Jesserun E, et al. Early and persistent intraventricular conduction abnormalities and requirements for pacemaking after percutaneous replacement of the aortic valve. J Am Coll Cardiol Intv 2008;1:310–6.
3. Nuis RJ, Van Mieghem NM, Schultz CJ, et al. Timing and potential mechanisms of new conduction abnormalities during the implantation of the Medtronic CoreValve System in patients with aortic stenosis. Eur Heart J 2011;32:2067–74.
4. El-Khally Z, Thibault B, Staniloae C, et al. Prognostic significance of newly acquired bundle branch block after aortic valve replacement. Am J Cardiol 2004;94:1008–11.
5. Zannad F, Huvelle E, Dickstein K, et al. Left bundle branch block as a risk factor for progression to heart failure. Eur J Heart Fail 2007;9:7–14.
6. Urena M, Mok M, Serra V, et al. Predictive factors and long-term clinical consequences of persistent left bundle branch block following transcatheter aortic valve implantation with a balloon-expandable valve. J Am Coll Cardiol 2012;60:1743–52.
7. Jilaihawi H, Chin D, Vasa-Nicotera M, et al. Predictors for permanent pacemaker requirement after transcatheter aortic valve implantation with the CoreValve bioprosthesis. Am Heart J 2009;157:860–6.
8. Fraccaro C, Buja G, Tarantini G, et al. Incidence, predictors, and outcome of conduction disorders after transcatheter self-expandable aortic valve implantation. Am J Cardiol 2011;107:747–54.
9. Guetta V, Goldenberg G, Segev A, et al. Predictors and course of high-degree atrioventricular block after transcatheter aortic valve implantation using the CoreValve revalving system. Am J Cardiol 2011;108:1600–5.
10. Tzikas A, van Dalen BM, Van Mieghem NM, et al. Frequency of conduction abnormalities after transcatheter aortic valve implantation with the Medtronic-CoreValve and the effect on left ventricular ejection fraction. Am J Cardiol 2011;107:285–9.
11. Chorianopoulos E, Krumsdorf U, Pleger ST, Katus HA, Bekeredjian R. Incidence of late occurring bradyarrhythmias after TAVI with the self-expanding CoreValve® aortic bioprosthesis. Clin Res Cardiol 2011;101:349–55.
12. Calvi V, Conti S, Pruiti GP, et al. Incidence rate and predictors of permanent pacemaker implantation after transcatheter aortic valve implantation with self-expanding CoreValve prosthesis. J Interv Card Electrophysiol 2012;34:189–95.
13. Muñoz-García AJ, Hernández-García JM, Jiménez-Navarro MF, et al. Changes in atrioventricular conduction and predictors of pacemaker need after percutaneous implantation of the CoreValve® aortic valve prosthesis. Rev Esp Cardiol 2010;63:1444–51.
14. Aktug O, Dohmen G, Brehmer K, et al. Incidence and predictors of left bundle branch block after transcatheter aortic valve implantation. Int J Cardiol 2012;160:26–30.
15. Gutiérrez M, Rodés-Cabau J, Bagur R, et al. Electrocardiographic changes and clinical outcomes after transapical aortic valve implantation. Am Heart J 2009;158:302–8.
16. Godin M, Eltchaninoff H, Furuta A, et al. Frequency of conduction disturbances after transcatheter implantation of an Edwards Sapien aortic valve prosthesis. Am J Cardiol 2010;106:707–12.
17. Sinhal A, Altwegg L, Pasupati S, et al. Atrioventricular block after transcatheter balloon expandable aortic valve implantation. J Am Coll Cardiol Intv 2008;1:305–9.
18. Roten L, Wenaweser P, Delacrétaz E, et al. Incidence and predictors of atrioventricular conduction impairment after transcatheter aortic valve implantation. Am J Cardiol 2010;106:1473–80.
19. Erkapic D, Kim WK, Weber M, et al. Electrocardiographic and further predictors for permanent pacemaker requirement after transcatheter aortic valve implantation. Europace 2010;12:1188–90.
20. El-Menyar AA, Abdou SM. Impact of left bundle branch block and activation pattern on the heart. Expert Rev Cardiovasc Ther 2008;6:843–57.
21. Sweeney MO, Hellkamp AS, Ellenbogen KA, et al. Adverse effect of ventricular pacing on heart failure and atrial fibrillation among patients with normal baseline QRS duration in a clinical trial of pacemaker therapy for sinus node dysfunction. Circulation 2003;107:2932–7.
22. Wilkoff BL, Cook JR, Epstein AE, et al. Dual-chamber pacing or ventricular backup pacing in patients with an implantable defibrillator: the Dual Chamber and VVI Implantable Defibrillator (DAVID) trial. JAMA 2002;288:3115–23.

Key Words: intraventricular conduction disturbances ▪ left bundle branch block ▪ pacemaker ▪ transcatheter aortic valve implantation.